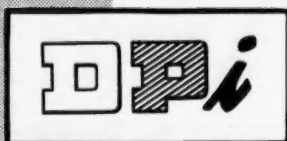


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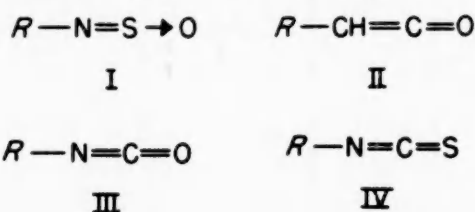
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THIONYLAMINES

By KENNETH C. KENNARD*

Thionylamines (I) are related structurally, by virtue of their terminal cumulated unsaturation, to ketenes (II), isocyanates (III), and isothiocyanates (IV).



Thionylamines are substituted imides of sulfurous acid and are analogues of isocyanates (substituted imides of carbonic acid). Thus, the two series resemble each other in some respects, notably in their mode of preparation and in their reaction with organometallic compounds.

Apparently, the first recorded preparation of a thionylamine was by Böttlinger (3), in 1878. He identified aniline hydrochloride from the reaction of thionyl chloride and aniline and he isolated, but did not identify, the other product, a "dark oil." About ten years later, Michaelis characterized thionylaniline and recognized in its preparation a general reaction which he extended to include about 75 amines. During the following decade, he directed so thorough a study of thionylamines that little synthetic work remained to be done. In several random cases where thionylamines were prepared in these Laboratories, the reproducibility of Michaelis's early work was found to be excellent.

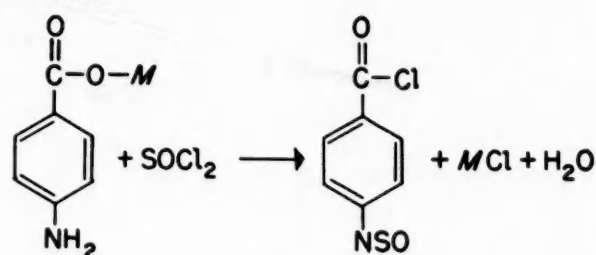
The most general synthesis involves

the reaction of thionyl chloride with the amine, usually in the presence of a hydrocarbon or ether as the solvent. (This



reaction is reminiscent of the synthesis of isocyanates by the reaction of amines with phosgene.) In the aliphatic series, a molar ratio of amine to thionyl chloride of three to one is used. In the aromatic series, the reaction may be carried out similarly or the amine hydrochloride may be used. In the latter case, an excess of thionyl chloride is employed, and the solution is boiled until the hydrogen chloride evolution has effectively ceased.

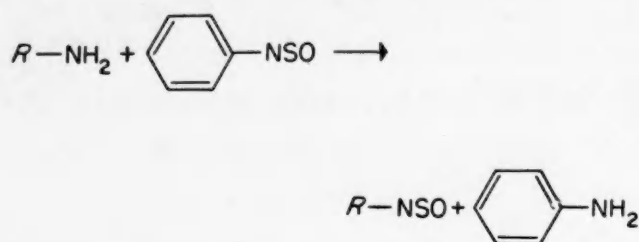
Aromatic amino acids react with thionyl chloride to give, in part, amides which result from the reaction of the by-product, carboxylic acid chloride, with the amine group of another molecule. This tendency may be overcome by using the lead or silver salt of the amino acid (1).



A synthesis which avoids side reactions, such as the chlorination of carboxylic acids or salt formation with other basic centers in the molecule, involves the disproportionation reaction between

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the desired amine and thionylaniline (10). Presumably, the reacting amine

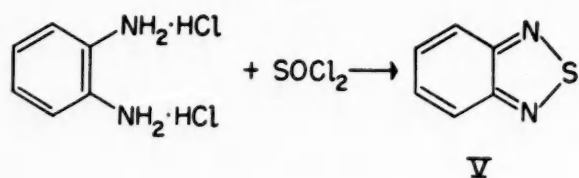


must possess characteristics which are sufficiently different from those of aniline that the disproportionation will take place nearly completely. Obviously, a means of separating the thionylamine from the starting materials and the other product, aniline, must also be available.

In a few isolated cases (hydrazines), the thionylamine has been prepared from the amine and sulfur dioxide.

Although much of the older literature contains no reference to yields, it is apparent that, in many cases, they are high, particularly among the simpler compounds. However, thionylamine formation is by no means restricted to simple molecules. The generality of this series may be realized by a study of References 1, 2, 4, 6, 8-12, and 14, which describe the known thionylamines, of which there are about 100.

Although meta- and paraphenylenediamine react normally with thionyl chloride to give meta- and paradithionylaminobenzene, the orthodiamine reacts with either thionyl chloride, thionylaniline, or sulfur dioxide to produce 2-thia-1,3-diazaindene (2,1,3-benzothiadiazole) (V) (in the older literature called "piazthiol") (10). Substituted



o-phenylenediamines and 1,2-diaminonaphthalene also give this reaction (10).

Apparently, benzylamine reacts anomalously with thionyl chloride to give benzaldehyde and benzylamine hydrochloride. Benzaldehyde or benzalaniline also

result from the reaction of thionylaniline and benzylamine (10). Similar reactions are reported for benzhydramine and for the xylylamines (11).

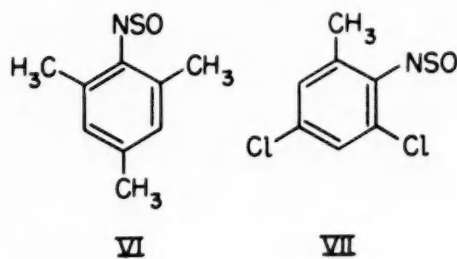
Aminophenols evidently do not form thionylamines by the use of thionyl chloride (10). However, alkylated aminophenols, e.g., the anisidines, do.

Aliphatic thionylamines are colorless liquids of acrid, pungent odor which fume in moist air. The boiling point of the thionylamine is generally 50° to 65° higher than that of the amine, the increment decreasing with increasing molecular weight of the amine. The aromatic members are colored solids or deep red oils, the depth of color depending to some extent on the other ring substituents. This series possesses an aromatic, not unpleasant, odor and generally boils from 6° to 25° higher than the parent amine.

In general, thionylamines react in aqueous solution to give the amine and sulfur dioxide (10). The reaction is in-



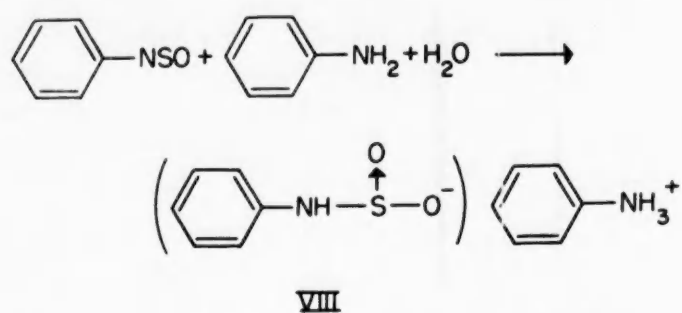
fluenced greatly by the solubility and structure of the amine (2, 10). Lower-molecular-weight aliphatic thionylamines are very unstable in the presence of water, while higher-molecular-weight aliphatic and aromatic ones are more stable. Hindered aromatic members, such as thionylmesidine (VI) and 3,5-dichloro-2-thionylaminotoluene (VII), may be steam-distilled without appreciable decomposition. In any case, aque-



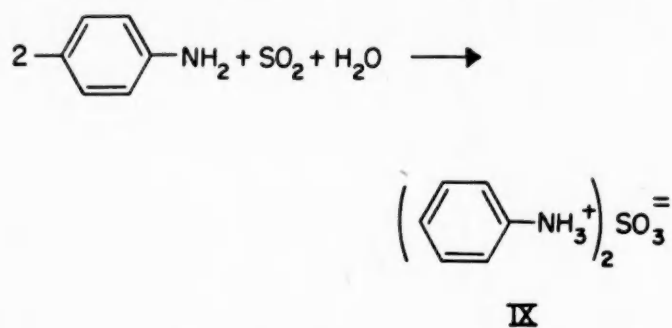
ous acid or base decomposes thionylamines rapidly.

Michaelis reported the reaction of thionylaniline with equimolar quantities of aniline and water to give an unstable

white solid (VIII), as follows (11):



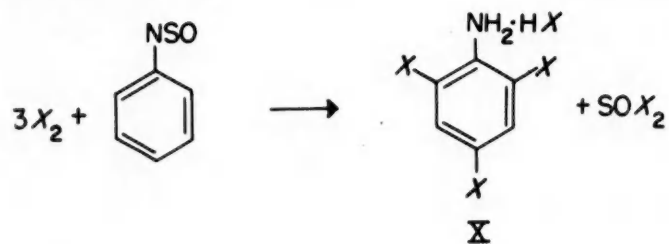
This reaction has not been verified and, indeed, subsequent work has established the veracity of the following reaction (7):



Compound IX was found to resemble Michaelis's white compound in all particulars. The very unstable nature of the acid and normal anilinium sulfites very probably contributed to the failure of the early workers to characterize them properly.

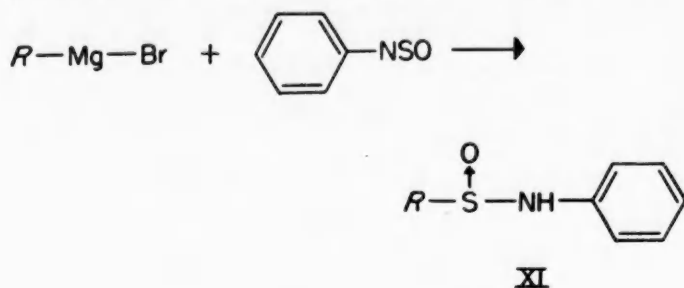
Michaelis also reported the formation of a general derivative of thionylamines (11). Formation of this derivative requires the heating together of equimolar quantities of thionylamine, the amine, benzaldehyde, and water. The structure postulated resembles that of the nonexistent compound, VIII. Consequently, reasonable doubt exists concerning the structure of these derivatives.

Bromine and chlorine react with thionylaniline, forming the trihaloaniline (X) (10, 11).



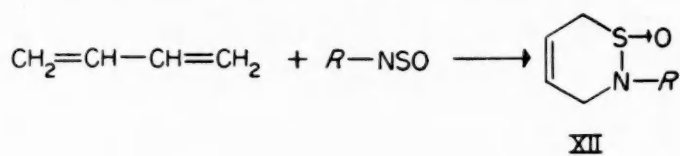
Thionylaniline, by reaction with organometallic compounds, affords a synthesis of sulfinanilides (5). Gilman and

co-workers (5) reported 80 and 61 percent yields for the reactions in which R = phenyl and benzyl, respectively, while

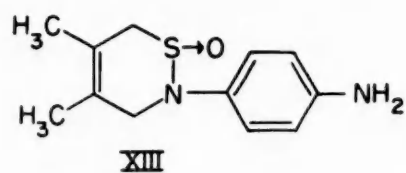


other workers reported slightly lower yields (13). For the case where R = ethyl, a 37 percent yield is recorded (13). The general reaction of thionylamines and Grignard reagents is analogous to the reaction of isocyanates and Grignard reagents. Lithium aryls react similarly; thus, phenyllithium and α -naphthyllithium have been employed to prepare sulfinanilides (XI), where R = phenyl and α -naphthyl, respectively (12).

Recently, a Diels-Alder type of reaction leading to a hitherto unknown heterocycle was reported (14). Butadiene and 2,3-dimethylbutadiene reacted with various aromatic thionylamines to produce 2,3-dihydro-6*H*-1,2-thiazine-1-oxides (XII). *p*-Dithionylaminobenzene re-



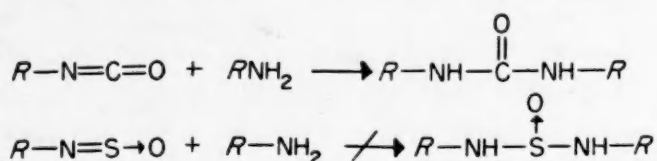
acted once with 2,3-dimethylbutadiene, and, with subsequent hydrolysis of the remaining thionylamino function, afforded 4,5-dimethyl-2-(4-aminophenyl)-2,3-dihydro-6*H*-1,2-thiazine-1-oxide (XIII).



The yields were reported to range from 40 to 88 percent for the thionylamines used. The reactions were carried out simply by heating the diene and the thionylamine together, without a solvent, for several hours. These adducts may become of considerable importance

because they can readily be converted to pyrrolidine derivatives.

The most apparent dissimilarity between isocyanates and thionylamines involves their behavior towards amines. This difference may be represented schematically thus:



Whereas isocyanates readily produce amides of carbonic acid (ureas), thionylamines either do not react at all, or undergo an interchange of radicals, as shown at the bottom of p. 2 (II).

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